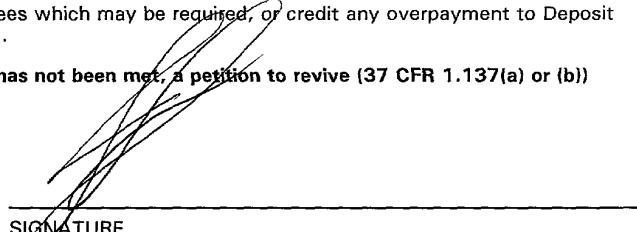


U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (Rev. 12-29-99)		ATTORNEY'S DOCKET NUMBER <b>022701-907</b>
<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371</b>		U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) <b>09/719839</b> Unassigned
INTERNATIONAL APPLICATION NO. <b>PCT/FR99/01442</b>	INTERNATIONAL FILING DATE <b>16 June 1999</b>	PRIORITY DATE CLAIMED <b>16 June 1998</b>
TITLE OF INVENTION <b>METHOD FOR PREPARING P-HYDROXYMANDELIC COMPOUNDS OPTIONALLY SUBSTITUTED</b>		
APPLICANT(S) FOR DO/EO/US <b>Isabelle JOUVE; Frederic FOURNET; Jean FRAGNON</b>		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<p>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and the PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))</p> <ol style="list-style-type: none"> <li><input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</li> <li><input checked="" type="checkbox"/> has been transmitted by the International Bureau.</li> <li><input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US)</li> </ol> <p>6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))</p> <ol style="list-style-type: none"> <li><input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li> <li><input type="checkbox"/> have been transmitted by the International Bureau.</li> <li><input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li><input type="checkbox"/> have not been made and will not be made.</li> </ol> <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p>		
Items 11. to 16. below concern other document(s) or information included:		
<p>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment.</p> <p><input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input type="checkbox"/> Other items or information:</p>		

U.S. APPLICATION NO. (If known, see 37 CFR 1.10) Unassigned <b>097719839</b>		INTERNATIONAL APPLICATION NO. PCT/FR99/01442	ATTORNEY'S DOCKET NUMBER 022701-907																				
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS	PTO USE ONLY																				
<b>Basic National Fee (37 CFR 1.492(a)(1)-(5)):</b> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO ..... \$1,000.00 (960) International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO ..... \$860.00 (970) International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$710.00 (958) International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... \$690.00 (956) International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ..... \$100.00 (962)																							
<b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b>		\$ 860.00																					
Surecharge of <b>\$130.00 (154)</b> for furnishing the oath or declaration later than months from the earliest claimed priority date (37 CFR 1.492(e)). 20 <input type="checkbox"/> 30 <input type="checkbox"/>		\$																					
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left; padding: 2px;">Claims</th> <th style="text-align: left; padding: 2px;">Number Filed</th> <th style="text-align: left; padding: 2px;">Number Extra</th> <th style="text-align: left; padding: 2px;">Rate</th> <th style="text-align: left; padding: 2px;"></th> </tr> </thead> <tbody> <tr> <td style="padding: 2px;">Total Claims</td> <td style="padding: 2px;">26 -20 =</td> <td style="padding: 2px;">0</td> <td style="padding: 2px;">X \$18.00 (966)</td> <td style="padding: 2px;">\$ 0</td> </tr> <tr> <td style="padding: 2px;">Independent Claims</td> <td style="padding: 2px;">1 -3 =</td> <td style="padding: 2px;">0</td> <td style="padding: 2px;">X \$80.00 (964)</td> <td style="padding: 2px;">\$ 0</td> </tr> <tr> <td colspan="3" style="padding: 2px;">Multiple dependent claim(s) (if applicable)</td> <td style="padding: 2px;">+ \$270.00 (968)</td> <td style="padding: 2px;">\$</td> </tr> </tbody> </table>		Claims	Number Filed	Number Extra	Rate		Total Claims	26 -20 =	0	X \$18.00 (966)	\$ 0	Independent Claims	1 -3 =	0	X \$80.00 (964)	\$ 0	Multiple dependent claim(s) (if applicable)			+ \$270.00 (968)	\$	<b>TOTAL OF ABOVE CALCULATIONS =</b>	\$ 860.00
Claims	Number Filed	Number Extra	Rate																				
Total Claims	26 -20 =	0	X \$18.00 (966)	\$ 0																			
Independent Claims	1 -3 =	0	X \$80.00 (964)	\$ 0																			
Multiple dependent claim(s) (if applicable)			+ \$270.00 (968)	\$																			
Reduction for 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).		\$																					
		<b>SUBTOTAL =</b>	\$ 860.00																				
Processing fee of <b>\$130.00 (156)</b> for furnishing the English translation later than months from the earliest claimed priority date (37 CFR 1.492(f)). 20 <input type="checkbox"/> 30 <input type="checkbox"/>		\$																					
		<b>TOTAL NATIONAL FEE =</b>	\$ 860.00																				
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 (581) per property +		\$																					
		<b>TOTAL FEES ENCLOSED =</b>	\$ 860.00																				
		Amount to be: refunded	\$																				
		charged	\$																				
a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>860.00</u> to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. <u>02-4800</u> in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>02-4800</u> . A duplicate copy of this sheet is enclosed.																							
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.																							
SEND ALL CORRESPONDENCE TO:  Norman H. Stepno BURNS, DOANE, SWECKER & MATHIS, L.L.P. P.O. Box 1404 Alexandria, Virginia 22313-1404 (703) 836-6620																							
SIGNATURE  Teresa Stanek Rea NAME 30,427 REGISTRATION NUMBER																							

09/719839  
526 Rec'd PCT/PTO 18 DEC 2000

Patent  
Attorney's Docket No. 022701-907

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of )  
Isabelle JOUVE et al. ) Group Art Unit: Unassigned  
Application No.: Unassigned ) Examiner: Unassigned  
(Corresponds to PCT/FR99/01442) )  
International Filing Date: 16 June 1999 )  
For: METHOD FOR PREPARING P- )  
HYDROXYMANDELIC COMPOUNDS )  
OPTIONALLY SUBSTITUTED )

**PRELIMINARY AMENDMENT**

**BOX PCT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-captioned application as follows:

**IN THE CLAIMS:**

Kindly amend the claims as follows.

Kindly cancel claim 1, without prejudice or disclaimer and insert claim 27, in lieu  
thereof:

Claim 2, line 1, change "1" to --27-- and change "characterised in that" to  
--wherein--;

line 15, delete "preferably a fluorine, chlorine or bromine atom,".

Claim 3, line 1, change "either claim 1 or claim 2" to --claim 27-- and change "characterised in that" to --wherein--;  
lines 6-7, delete "and preferably from 1 to 4 carbon atoms, ";  
lines 8-9, delete "preferably from 1 to 4 carbon atoms, ".

Claim 4, line 1, change "one of claims 1 to 3" to --claim 27-- and change "characterised in that" to --wherein--;  
line 5, delete "preferably".

Claim 5, line 1, change "one of claims 1 to 4" to --claim 27-- and change "characterised in that" to --wherein--;  
line 3, after "guetol," insert --and--.

Claim 6, line 1, change "one of claims 1 to 5" to --claim 27-- and change "characterised in that" to --wherein--.

Claim 7, line 1, change "characterised in that" to --wherein--.

Claim 8, line 1, change "characterised in that" to --wherein--;  
line 3, delete "preferably";  
line 4, delete ", generally 1 to 3 unsaturations";

lines 15-16, delete "preferably a fluorine, chlorine or bromine atom, ".

Claim 9, line 1, change "characterised in that" to --wherein--;  
lines 2-3, delete "an aromatic hydrocarbon residue, and, in particular, ";  
line 7, delete "preferably from 0 to 3, ".

Claim 10, line 1, change "characterised in that" to --wherein--.

Claim 11, line 1, change "characterised in that" to --wherein--;  
lines 3-4, delete ", generally having 3 to 7 carbon atoms, preferably 6 carbon atoms, in the ring".

Claim 12, line 1, change "one of claims 6 to 11" to --claim 6-- and change "characterised in that" to --wherein--.

13. (Amended) A process according to claim 6, [characterised in that] wherein the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II) selected from the group consisting of:

[- dicarboxylic aliphatic acids, such as:]

. oxalic acid

- . malonic acid
- . succinic acid
- . glutaric acid
- . adipic acid
- . 2,4-dimethyl adipic acid
- . pimelic acid
- . suberic acid
- . azelaic acid
- . sebacic acid
- . dodecane dioic acid
- . fumaric acid
- . maleic acid

[- cycloalkanedicarboxylic acids, such as]

- . cyclohexane 1,4-dicarboxylic acid,

[- aromatic dicarboxylic acids, such as:]

- . phthalic acid
- . isophthalic acid
- . terephthalic acid
- . phenylenediacetic acid
- . naphthalene 1,5-dicarboxylic acid
- . naphthalene 1,6-dicarboxylic acid
- . 4,4'-diphenylcarboxylic acid

- . 3,3'-diphenylcarboxylic acid
- . bis(4-hydroxycarbonyl) phenyl oxide
- . bis(3-hydroxycarbonyl) phenyl oxide
- . 4,4'-dihydroxycarbonyl diphenylsulphone
- . 3,3'-dihydroxycarbonyl diphenylsulphone
- [ - ] . pyrimidine or imidazole dicarboxylic acids.
- [ - ] aminopolycarboxylic acids:
  - . ethylenediaminetetraacetic acid (E.D.T.A.)
  - . diethylenetriaminopentacetic acid (D.T.P.A.)
  - . nitrilotriacetic acid (N.T.A.) and
  - . N-(2-hydroxyethyl)ethylene diaminotriacetic acid (H.E.D.T.A.).

Claim 14, line 1, change "one of claims 1 to 13" to --claim 27-- and change "characterised in that" to --wherein--;  
line 2, delete ", in particular from 0.1 to 3% acetic acid".

Claim 15, line 1, change "one of claims 1 to 14" to --claim 27-- and change "characterised in that" to --wherein--;  
lines 2-3, delete ", preferably in the region of 50% by weight".

Claim 16, line 1, change "one of claims 1 to 15" to --claim 27-- and change "characterised in that" to --wherein--;

line 3, delete "and is preferably selected between 2.0 and 3.0".

Claim 17, line 1, change "one of claims 1 to 16" to --claim 27-- and change "characterised in that" to --wherein--.

Claim 18, line 1, change "one of claims 1 to 17" to --claim 27-- and change "characterised in that" to --wherein--;

line 2, delete "preferably comprised";

line 3, delete ", and more particularly in the region of 1 mole/litre".

Claim 19, line 1, change "one of claims 1 to 18" to --claim 27-- and change "characterised in that" to --wherein--;

line 3, delete ", and preferably between 0.01 and 0.02".

Claim 20, line 1, change "one of claims 1 to 19" to --claim 27-- and change "characterised in that" to --wherein--;

lines 3-4, delete ", preferably between 1 and 2%".

Claim 21, line 1, change "one of claims 1 to 20" to --claim 27-- and change "characterised in that" to --wherein--.

Claim 22, line 1, change "characterised in that" to --wherein--;

line 2, delete "preferably between 1.2 and 2.6%,".

Claim 23, line 1, change "one of claims 1 to 22" to --claim 27-- and change "characterised in that" to --wherein--.

Claim 24, line 1, change "one of claims 1 to 23" to --claim 27-- and change "characterised in that" to --wherein--;  
line 2, delete ", preferably between 30°C and 40°C".

25. (Amended) [Use of the optionally substituted p-hydroxymandelic compounds obtained according to one of claims 1 to 24 as intermediates] An intermediate for the production of hydroxyarylacetic acids, hydroxyarylglyoxylic acids, or hydroxyaromatic aldehydes comprising using the optionally substituted p-hydroxymandelic compounds obtained according to the process of claim 27.

26. (Amended) [Use of p-hydroxymandelic acid and 3-methoxy p-hydroxymandelic, 3-ethoxy p-hydroxymandelic acids or 3-isopropoxy p-hydroxymandelic acids obtained in accordance with the preparation process described in one of claims 1 to 24] A process for the production of 4-hydroxy benzaldehyde and vanillin and analogues by oxidation of said acids using p-hydroxymandelic acid and 3-methoxy p-hydroxymandelic acid, 3-ethoxy p-hydroxymandelic acid, or 3-isopropoxy p-hydroxymandelic acid obtained in accordance with claim 27.

--27. A process for the preparation of an optionally substituted p-hydroxymandelic compound, comprising condensing, in water and in the presence of an alkaline agent, (1) a hydroxylated aromatic compound with (2) glyoxylic acid, the para-position of said hydroxylated aromatic compound being free and said condensation being carried out in the presence of a catalytically effective amount of (3) a polycarboxylic compound.--

**REMARKS**

Entry of the foregoing amendment(s) is respectfully requested.

The claims have been amended to eliminate multiple dependency and to place them in better condition for U.S. patent practice.

Should the Examiner have any questions concerning the subject application, a telephone call to the undersigned would be appreciated.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By:

Teresa Stanek Rea  
Registration No. 30,427

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

Date: December 18, 2000

WO 99/65853

PCT/FR99/01442

A PROCESS FOR THE PREPARATION  
OF OPTIONALLY SUBSTITUTED P-HYDROXYMANDELIC COMPOUNDS

A subject of the present invention is a process for the preparation of optionally substituted p-hydroxymandelic compounds and derivatives.

In the disclosure of the invention which follows, the term, "optionally substituted p-hydroxymandelic compounds" is used to refer to an aromatic compound which carries at least one  $-CHOH-COOH$  group in para position of a hydroxyl group.

The present invention relates, more particularly, to the preparation of p-hydroxymandelic acid and 3-methoxy p-hydroxymandelic acid.

One of the conventional synthesis routes for p-hydroxymandelic acids consists in carrying out the condensation, in alkaline medium, of glyoxylic acid on phenol and/or its corresponding derivatives.

The yield is limited by the fact that the condensation reaction is not selective and also produces o-hydroxymandelic acids and dimandelic acids.

Furthermore, the reaction yield is reduced due to a parasitic secondary reaction. In fact, glyoxylic acid in aqueous alkaline medium is converted according to Cannizaro's reaction into oxalic and glycolic acids.

In order to prevent this Cannizaro's reaction from becoming dominant and destroying the glyoxylic acid, a proposal has been made in FR-A 2 132 364 for the condensation reaction to be carried out in a dilute aqueous medium and at low temperature or ambient temperature.

In view of the difficulty in obtaining satisfactory reaction yields, it is important to control the various parameters of the process, and, in particular, the quality of the glyoxylic acid used.

The most worthwhile process from an industrial viewpoint for the preparation of glyoxylic acid consists in oxidising the glyoxal with nitric acid. In this way, aqueous solutions of glyoxylic acid are obtained, which, in addition to unreacted glyoxal, also contain oxalic acid, organic acids, such as formic acid, acetic acid, glycolic acid, and nitric acid.

Until now, new methods have been constantly sought for the separation and purification of glyoxylic acid.

Therefore, a process was proposed in DE-A 1 198 339 which first and foremostly permitted the nitric acid to be eliminated, followed by the oxalic acid using basic ion exchange resins, followed by the glyoxal and the other impurities by over-concentration of the solution and crystallisation.

In DE-A 2 501 743, a process was disclosed in which the glyoxylic acid is separated from these impurities by extraction using aliphatic or cycloaliphatic alcohols, or aliphatic esters of alcohols with low carbon condensation.

A process for obtaining aqueous solutions of glyoxylic acid free from other acids has also been described in FR-A 2 552 426 which consists in treating the starting solution with an organic nitrogenous compound, preferably a tertiary amine, at a temperature which is at the most equal to 50°C, then in extracting the glyoxylic acid by extraction of the organic phase with water, at a higher temperature.

A constant concern has therefore been noted in the prior art of providing a solution of glyoxylic acid which is free of impurities.

Running counter to this teaching, it has been found that within the scope of preparing optionally substituted p-hydroxymandelic compounds condensation of glyoxylic acid and of the corresponding phenol is carried out with an increased yield, provided that said reaction is carried out in the presence of a dicarboxylic acid used in a certain quantity.

A precise subject of the present invention is a process for the preparation of optionally substituted p-hydroxymandelic compounds and derivatives, which consists in carrying out the condensation, in water, in the presence of an alkaline agent, of an aromatic carrier compound

with at least one hydroxyl group and the para position of which is free, with glyoxylic acid, said process being characterised in that the reaction is carried out in the presence of an effective quantity of a carrier compound with at least two carboxylic functions.

In accordance with the process of the invention, the use of a catalyst according to the invention allows the reaction yield to be increased.

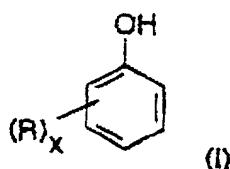
Another advantage of the process according to the invention is that it can involve a more technical glyoxylic acid containing, *inter alia*, oxalic acid.

The process according to the invention is used, most particularly, with phenol but also with substituted phenols which have at least one non-substituted para position.

The aromatic nucleus carries at least one hydroxyl group, but it can also carry one or more other substituents. Generally, "several substituents" means less than four substituents per aromatic nucleus.

Any substituent can be present provided that it is does not interfere in the reaction of the invention.

Therefore, the process according to the invention is well suited for use with hydroxylated aromatic compounds corresponding to the following formula (I):



in which formula (I):

- the para position is free,
- x is an integer between 1 and 4,
- R represents :
  - a hydrogen atom,

- a hydrocarbon group having from 1 to 20 carbon atoms selected from the alkyl, alkoxy, hydroxyalkyl, cycloalkyl, aryl, phenoxy, alkoxyalkyl, fluoroalkyl, hydroxyalkoxyalkylene groups,
- a hydroxyl group,
- a -CHO group,
- an acyl group having from 2 to 6 carbon atoms,
- a halogen atom, preferably a fluorine, chlorine or bromine atom,
- two R groups placed on two vicinal carbon atoms can form together and with the carbon atoms which carry them a benzene ring.

Examples of R radicals which are capable of being carried by the aromatic nucleus are given hereinafter:

- alkyl radicals, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, n-octyl, 2-ethyl hexyl, decyl, octadecyl, eicosyl,
- alkoxy radicals, such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, hexyloxy, decyloxy, hexadecyloxy, octadecyloxy, or a phenoxy radical,
- hydroxyalkyl radicals, such as hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxyhexyl, hydroxydecyl,
- cycloalkyl radicals, such as cyclopentyl, cyclohexyl, cycloheptyl,
- fluoroalkyl radicals, such as fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, 1,1,1-trifluoro ethyl, pentafluoroethyl, fluoropropyl, fluorobutyl, trifluoroamyl,
- hydroxyalkoxyalkylene radicals, such as hydroxymethoxyethylene, hydroxyethyl di-(oxyethylene), hydroxyethyl tri-(oxyethylene), 1,2-hydroxyethoxypropylene, hydroxyethoxybutylene, hydroxypropoxypropylene, hydroxybutyloxybutylene, hydroxybutyl di-(oxybutylene),
- halogen atoms, such as fluorine, chlorine, bromine, or iodine.

Quite preferably, hydroxylated aromatic compounds are used in the process of the invention, corresponding to the general formula (I), in which:

- x is equal to 0, 1, 2 or 3,
- R represents one of the following groups or functions:
  - . a hydrogen atom,

- . a linear or branched alkyl radical having from 1 to 10 carbon atoms, and preferably from 1 to 4 carbon atoms,
- . a linear or branched alkoxy radical having from 1 to 10 carbon atoms, preferably from 1 to 4 carbon atoms,
- . an -OH group,
- . a -CHO group,
- . a halogen atom,
- . a -CF<sub>3</sub> group.

Still more preferably, the compounds of formula (I) are selected in which the R radicals which are identical or different are a hydrogen atom, a linear or branched alkyl radical with 1 to 4 carbon atoms, such as the methyl, ethyl, n-propyl, isopropyl, n-butyl or isobutyl radicals, a linear or branched alkoxy radical having 1 to 4 carbon atoms, such as the methoxy or ethoxy radicals, a -CHO group, or a chlorine atom, and x is preferably equal to 0 or 1.

By way of illustration of compounds corresponding to formula (I), the following can be mentioned:

- those corresponding to formula (I) in which x is equal to 0, such as phenol,
- those corresponding to formula (I) in which x is equal to 1, such as
  - . pyrocatechin
  - . resorcin
  - . o-cresol
  - . m-cresol
  - . 2-ethyl phenol
  - . 3-ethyl phenol
  - . 2-propyl phenol
  - . 2-sec-butyl phenol
  - . 2-tert-butyl phenol
  - . 3-tert-butyl phenol
  - . 2-methoxy phenol (guaiacol)
  - . 3-methoxy-phenol
  - . 2-ethoxy phenol (guetol)
  - . 2-isopropoxy phenol
  - . salicylic aldehyde

- . methyl salicylate
- . 2-chloro phenol
- . 3-chloro phenol
- . 3-nitro phenol
- those corresponding to formula (I) in which x is equal to 2, such as:
  - . 2,3-dimethyl phenol
  - . 2,5-dimethyl phenol
  - . 3,5-dimethyl phenol
  - . 2-hydroxy 5-acetamido benzaldehyde
  - . 2-hydroxy 5-ethamido benzaldehyde
  - . 2,3-dichloro phenol
  - . 2,5-dichloro phenol
  - . 3,5-dichloro phenol
  - . pyrogallol
- those corresponding to formula (I) in which x is equal to 3, such as:
  - . 2,3,5-trimethyl phenol
  - . 3,5-di-tert butyl phenol
  - . 2,3,5-trichloro phenol
- those corresponding to formula (I) having a naphthalenic radical, such as:
  - . 1-naphthol
  - . 2-naphthol
  - . 1,2-dihydroxy naphthalene
  - . 1,5-dihydroxy naphthalene
  - . 2,3-dihydroxy naphthalene
  - . 2,6-dihydroxy naphthalene
  - . 2,7-dihydroxy naphthalene
  - . 6-bromo 2-naphthol
- those corresponding to formula (I) having a chain formation of benzene nuclei:
  - . 2-phenoxy phenol
  - . 3-phenoxy phenol

Of the list of afore-mentioned compounds, the aromatic carrier compounds preferably used which have at least one hydroxyl group are: phenol, o-cresol, m-cresol, 3-ethyl phenol, 2-tert-butyl phenol, guaiacol, guetol.

As regards the type of catalyst used, an at least difunctional acid can be used which corresponds to the following formula (II):



in which formula (II),  $\text{R}_1$  represents a valency bond or an optionally substituted hydrocarbon radical containing 1 to 40 carbon atoms.

To be more exact, in formula (II),  $\text{R}_1$  symbolises a substituted or non-substituted hydrocarbon radical which can be a linear or branched, saturated or unsaturated acyclic aliphatic radical; a monocyclic or polycyclic, saturated, unsaturated, or aromatic carbocyclic radical; a monocyclic or polycyclic, saturated, unsaturated or aromatic heterocyclic radical.

The carrier compounds with at least two carboxylic functions of general formula (II) in which  $\text{R}_1$  represents a valency bond or a divalent radical preferably having 1 to 15 carbon atoms are quite particularly suitable for implementation of the process according to the invention.

The carrier compounds with at least two carboxylic functions of general formula (II) in which  $\text{R}_1$  represents a linear or branched, saturated or unsaturated aliphatic residue are particularly well suited for use of the process according to the invention.

To be more exact,  $\text{R}_1$  represents a linear or branched, acyclic aliphatic residue having preferably 1 to 12 carbon atoms, saturated or containing one or more unsaturations on the chain, generally 1 to 3 unsaturations which can be single or conjugated double bonds, or triple bonds.

The hydrocarbon chain can optionally be:

- (1) - interrupted by one of the following groups called Y:  

$$\begin{array}{c} -\text{O}-; -\text{CO}-; -\text{COO}-; -\text{N}(\text{R}_2)-\text{CO}-\text{N}(\text{R}_2)-\text{S}-; -\text{SO}_2- \end{array}$$

in which formula  $\text{R}_2$  represents hydrogen or a linear or branched alkyl radical having 1 to 4 carbon atoms, preferably a methyl or ethyl radical, or a radical of  $-(\text{CH}_2)_p-\text{COOH}$  type in which  $p$  is a number between 1 and 5,

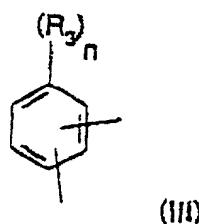
(2) - and/or bearing one of the following substituents:

- OH; - COOH ; - CHO ; - NO<sub>2</sub> ; - CN ; - NH<sub>2</sub> ; - SH ; - X ; CF<sub>3</sub>
- NH - [(CH<sub>2</sub>)<sub>p</sub> - COOH] or - N -[(CH<sub>2</sub>)<sub>p</sub> - COOH]<sub>2</sub>

with X representing a halogen atom, preferably a fluorine, chlorine or bromine atom, and p having the meaning given hereinabove.

The carrier compounds with at least two carboxylic functions of general formula (II) in which R<sub>1</sub> represents a monocyclic or polycyclic hydrocarbon residue are also suitable for implementation of the process according to the invention.

R<sub>1</sub> preferably represents an aromatic hydrocarbon residue, and, in particular, a benzene residue corresponding to the general formula (III):



in which formula (III):

- n is an integer from 0 to 4, preferably from 0 to 3,
- R<sub>3</sub> represents one of the following groups or functions,
  - . a hydrogen atom,
  - . a linear or branched alkyl radical having from 1 to 4 carbon atoms,
  - . a linear or branched alkoxy radical having from 1 to 4 carbon atoms,
  - . a methylene or ethylene dioxy radical,
  - . a -CHO group,
  - . a phenyl or benzyl radical,
  - . a halogen atom,

Even more preferably, the compounds of formula (II) are selected in which the R<sub>1</sub> radical corresponds to formula (III) in which the R<sub>3</sub> radicals, which are identical or different, are a hydrogen atom, a methyl radical, a methoxy radical, a -CHO group.

The carrier compounds having at least two carboxylic functions can correspond to general formula (II) in which the R<sub>1</sub> radical represents a polycyclic aromatic hydrocarbon divalent residue; the rings can form between themselves ortho condensed, ortho- and peri-condensed

systems. More particularly, a naphthylene residue can be mentioned; said rings being able to be substituted by 1 to 4 R<sub>3</sub> radicals, preferably by 1 to 3, R<sub>3</sub> having the meanings stated hereinabove for the substituents of the aromatic hydrocarbon residue of general formula (III).

In general formula (II) of the carrier compounds with at least two carboxylic functions, R<sub>1</sub> can also represent a carbocyclic residue which is saturated or which comprises 1 or 2 unsaturations in the ring, generally having from 3 to 7 carbon atoms, preferably 6 carbon atoms in the ring; said ring being able to be substituted by 1 to 5, preferably 1 to 3, R<sub>3</sub> radicals, R<sub>3</sub> having the meanings stated hereinabove for the substituents of the aromatic hydrocarbon residue of general formula (III).

As preferred examples of R<sub>1</sub> radicals the cyclohexane-diyl radicals can be mentioned which are optionally substituted by linear or branched alkyl radicals having 1 to 4 carbon atoms.

The carrier compounds with at least two carboxylic functions can also correspond to formula (II) in which R<sub>1</sub> represents a divalent radical constituted by a chain formation of two to four residues as defined hereinabove, an aliphatic residue, an aromatic residue, or a cycloaliphatic residue. These can be connected together by a valency bond or by a function group which can be, in particular, a group selected from the groups called Y.

Some examples of R<sub>1</sub> radicals are given hereinafter:

- CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-;
- CH<sub>2</sub>-CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-;
- CH<sub>2</sub>-O-C<sub>6</sub>H<sub>4</sub>-;
- CH<sub>2</sub>-O-C<sub>6</sub>H<sub>4</sub>-;
- CH<sub>2</sub>-O-C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-;
- C<sub>6</sub>H<sub>4</sub>-C<sub>6</sub>H<sub>4</sub>-;
- C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-;
- C<sub>6</sub>H<sub>4</sub>-O-C<sub>6</sub>H<sub>4</sub>-;
- CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-

The following carrier compounds with at least two carboxylic functions can be mentioned, quite particularly, by way of catalysts which are suitable for the present invention:

- dicarboxylic aliphatic acids, such as:

- . oxalic acid
- . malonic acid
- . succinic acid
- . glutaric acid
- . adipic acid
- . 2,4-dimethyl adipic acid
- . pimelic acid
- . suberic acid
- . azelaic acid
- . sebacic acid
- . dodecane dioic acid
- . fumaric acid
- . maleic acid

- cycloalkanedicarboxylic acids, such as cyclohexane 1,4-dicarboxylic acid,

- aromatic dicarboxylic acids, such as:

- . phthalic acid
- . isophthalic acid
- . terephthalic acid
- . phenylenediacetic acid
- . naphthalene 1,5-dicarboxylic acid
- . naphthalene 1,6-dicarboxylic acid
- . 4,4'-diphenylcarboxylic acid
- . 3,3'-diphenylcarboxylic acid
- . bis(4-hydroxycarbonyl) phenyl oxide
- . bis(3-hydroxycarbonyl) phenyl oxide
- . 4,4'-dihydroxycarbonyl diphenylsulphone
- . 3,3'-dihydroxycarbonyl diphenylsulphone

- pyrimidine or imidazole dicarboxylic acids.

In the afore-mentioned list of dicarboxylic acids, the compounds preferably used are: oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, sebacic acid, phthalic acid, isophthalic acid, terephthalic acid.

Aminopolycarboxylic acids are also perfectly well suited for implementation of the process according to the invention. As examples of aminopolycarboxylic acids suitable for use in the process of the invention mention can be made of the following, inter alia:

- . ethylenediaminetetraacetic acid (E.D.T.A.)
- . diethylenetriaminopentacetic acid (D.T.P.A.)
- . nitrilotriacetic acid (N.T.A.)
- . N-(2-hydroxyethyl)ethylene diaminotriacetic acid (H.E.D.T.A.)

Of the afore-mentioned aminopolycarboxylic acids, ethylenediaminetetraacetic acid is preferably selected.

According to the process of the invention, the reaction is carried out in the presence of an alkali metal hydroxide which can be sodium or potassium hydroxide.

For economic considerations, sodium hydroxide is preferably selected.

With regard to the concentrations and quantities of reagents to be used, the preferred conditions are defined hereinbelow.

In accordance with the process according to the invention a solution of glyoxylic acid is used. The concentration of said solution is not critical and can vary greatly, e.g. between 15 and 70% by weight. Preferably, commercial solutions are used, the concentration of which is approximately 50%.

According to the process of the invention, the glyoxylic acid is reacted on the excess of the hydroxylated aromatic compound of formula (I). The molar ratio between the hydroxylated aromatic compound of formula (I) and the glyoxylic acid varies between 1.5 and 4.0 and is preferably selected between 2.0 and 3.0.

The alkali metal hydroxide solution used has a concentration which is generally between 10 and 50% by weight. The concentration of the starting solution is not critical. However, as the concentration of the hydroxylated aromatic compound of formula (I) is advantageously low in the reaction medium, a dilute solution of alkali metal is used to carry out the dilution of the reaction medium.

The quantity of alkali metal hydroxide introduced into the reaction medium takes account of the quantity necessary to saponify the hydroxyl function of the hydroxylated aromatic compound of formula (I) and of the quantity necessary to saponify the carboxylic function of the glyoxylic acid.

If the hydroxylated aromatic compound of formula (I) has saponifiable functions other than the hydroxyl group, the quantity of alkali metal hydroxide necessary to saponify all the saponifiable functions which can be hydroxyl groups and/or COOH carboxylic functions is therefore introduced.

Generally, the quantity of alkali metal hydroxide can vary greatly and be equal to, or approximately equal to, the stoichiometry, or in excess. Generally, the quantity of alkali metal hydroxide varies between 80 and 120% of the stoichiometric quantity.

The concentration of the hydroxylated aromatic compound of formula (I) is preferably between 0.5 and 1.5 moles/litre, and, more particularly, in the region of 1 mole/litre.

With regard to the quantity of catalyst used, this is determined in such a way that the molar ratio between the catalyst and the hydroxylated aromatic compound of formula (I) is between 0.005 and 0.025, and preferably between 0.01 and 0.02.

The quantity of catalyst used, as expressed by the ratio between the number of moles of catalyst and the number of moles of glyoxylic acid is advantageously selected to be between 0.5 and 2.5%, preferably between 1 and 2%.

The preferred catalyst is oxalic acid.

The commercial solutions of glyoxylic acid can contain very low quantities of oxalic acid. The oxalic acid of the reaction can therefore be provided, in part, by the starting solution. In this case, it will be necessary to complete the quantity of oxalic acid by the addition of oxalic acid or of any other dicarboxylic acid in order that the afore-mentioned ratios are observed.

According to a preferred embodiment of the invention, a solution of glyoxylic acid is advantageously used containing between 0.6 and 3%, preferably between 1.2 and 2.6%, by weight of oxalic acid, expressed in relation to the weight of glyoxylic acid.

The reaction temperature is advantageously selected between 20°C and 60°C, and preferably between 30°C and 40°C.

The process according to the invention is carried out at atmospheric pressure, but under a controlled inert gas atmosphere, preferably nitrogen or rare gases, in particular nitrogen.

A preferred practical embodiment of the invention will be given hereinafter.

The solution of glyoxylic acid and catalyst, and, in parallel, the solution of alkali metal hydroxide employed in a quantity necessary to salify the COOH function are introduced into a reaction medium containing the hydroxylated aromatic compound of formula (I), water and the alkali metal hydroxide in a quantity necessary to salify the hydroxyl group and other possible salifiable functions of the compound of formula (I).

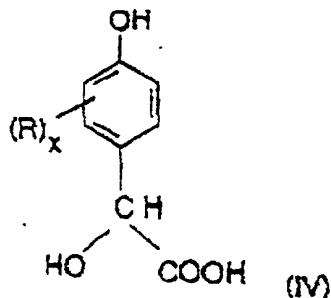
The reaction medium is kept under agitation and at the temperature selected within the afore-mentioned range for a variable period ranging from 1 to 10 hours.

Another variant of the execution of the invention consists in adding the reaction catalyst not to the aqueous solution of glyoxylic acid but simultaneously with the hydroxylated aromatic compound of formula (I).

At the end of the reaction, the optionally substituted p-hydroxymandelic acid obtained is separated in salified form using conventional separation techniques, in particular crystallisation.

The process according to the invention is quite particularly well suited when an aqueous solution of glyoxylic acid is used containing monofunctional acids, such as formic and glycolic acid, and, in particular, when acetic acid is present in a concentration which is variable between 0.1 and 3%.

The process according to the invention results in the production of optionally substituted p-hydroxymandelic compounds which can be represented by the following formula (IV):



in which formula (IV) R and x have the meaning given in formula (I).

These products are particularly worthwhile since they are intermediate products, which, *inter alia*, allow hydroxyarylacetic acids to be obtained by reduction and hydroxyarylglyoxylic (= hydroxyaryl  $\alpha$ -oxo acetic) acids or hydroxyaromatic aldehydes to be obtained by oxidation.

A preferred use of the invention is the preparation of hydroxyaromatic aldehydes by oxidation of the compounds of formula (IV) obtained according to the invention.

The oxidation of the compounds of formula (IV) can be carried out according to the techniques described in writings. Thus, reference can be made to P. HEBERT [Bull. Soc. Chim. France, 27, p. 45-55 (1920)] and to NAGAI SHIGEKI et al [JP-A 76/128934]. The oxidation is generally carried out using oxygen or air under pressure, in the presence of an appropriate catalyst, such as derivatives of chromium, cobalt, copper, vanadium or osmium, for example.

Therefore, the invention allows easy access to 4-hydroxy benzaldehyde and to vanillin and its analogues, e.g. 3-ethyl, 3-isopropyl vanillin, by oxidation respectively of p-hydroxymandelic acid and of 3-methoxy p-hydroxymandelic acids, and 3-ethoxy p-hydroxy-mandelic or 3-isopropoxy p-hydroxymandelic acids.

The following examples illustrate the invention, without however limiting it.

In the examples, the percentages stated are expressed by weight.

The abbreviations mentioned in the examples have the following meanings:

Conversion (TT) = 
$$\frac{\text{number of moles of guaiacol converted}}{\text{number of moles of guaiacol introduced}}$$

Yield (RR) = 
$$\frac{\text{number of moles of mandelic acid formed}}{\text{number of moles of mandelic acid introduced}}$$

Selectivity (RT) = 
$$\frac{\text{number of moles of mandelic acid formed}}{\text{number of moles of guaiacol converted}}$$

### Example 1

- 600 g distilled water,
- 91.6 g (0.687 mol) of a 30% aqueous soda solution,
- 93 g (0.750 mol) guaiacol

are introduced into a 1-litre glass reaction vessel equipped with a double jacket, a pH electrode, a temperature probe, a condenser, an inert gas supply, and a mechanical agitation device.

An inert atmosphere is established, and the reaction mixture is brought to 35°C, and 50.7 g (0.380 mol) of a 30% by weight aqueous soda solution and 55.2 g of a 50% by weight aqueous glyoxylic acid solution are added simultaneously over a period of 2 hours. Oxalic acid is added with the glyoxylic acid introduced in such a quantity that it represents 0.75% by weight of the glyoxylic acid solution.

The glyoxylic acid solution introduced contains 0.3% oxalic acid, 0.9% lower carboxylic acids such as acetic acid, and formic acid and glycolic acid in a respective quantity of less than 0.1%.

The reaction mixture is maintained at 35°C for 2 hours.

At the end of the reaction, the reaction products are analysed using high performance liquid chromatography.

The results obtained were as follows:

- conversion:
  - . TT = 47.3%
- 4-hydroxy 3-methoxy mandelic acid:
  - . RR = 79.7%
  - . RT = 84.2%
- 2-hydroxy 3-methoxy mandelic acid:
  - . RR = 4.8%
  - . RT = 5.1%
- 2-hydroxy 3-methoxy 1,5-dimandelic acid:
  - . RR = 8.0%
  - . RT = 4.0%

#### Comparative Example 2

Example 1 is reproduced, except that no oxalic acid is introduced.

The results obtained were as follows:

- conversion:
  - . TT = 46.1%
- 4-hydroxy 3-methoxy mandelic acid:
  - . RR = 76.9%
  - . RT = 83.0%
- 2-hydroxy 3-methoxy mandelic acid:
  - . RR = 5.1%
  - . RT = 5.5%
- 2-hydroxy 3-methoxy 1,5-dimandelic acid:
  - . RR = 7.5%
  - . RT = 4.1%

Example 3

In this example, Example 1 is reproduced except that a 50% solution of glyoxylic acid is used containing 0.4% by weight of oxalic acid.

The results obtained are as follows:

- conversion:

. TT = 48%

- 4-hydroxy 3-methoxy mandelic acid:

. RR = 79.3%

. RT = 83.1%

- 2-hydroxy 3-methoxy mandelic acid:

. RR = 5.6%

. RT = 5.8%

- 2-hydroxy 3-methoxy 1,5-dimandelic acid:

. RR = 8.0%

. RT = 4.2%

Examples 4 to 8

In the following set of examples Example 1 is reproduced except that different types of dicarboxylic acids are used, such as malonic acid, succinic acid and E.D.T.A.

The glyoxylic acid solution used contains oxalic acid at a rate of 0.09%, lower carboxylic acids such as acetic acid at a rate of 1%, formic acid and glycolic acid at respective quantities of less than 0.3%.

All the conditions of the examples and the results obtained are indicated in Table I.

Table 1

Ref. ex.	Dicarboxylic acid (%)	TT	RR			RT		
			para	ortho	di	para	ortho	di
4	-	45.2	77.5	4.9	7.6	84.3	5.3	4.1
5	oxalic acid (2.0%)	47.8	80.1	4.8	8.1	83.0	5.0	4.2
6	malonic acid (2.0%)	46.1	80.2	5.2	7.6	84.8	5.5	4.1
7	succinic acid (1.9%)	48.0	81.4	5.6	8.0	85.0	5.8	4.2
8	E.D.T.A. (1.5%)	44.5	80.6	4.9	7.7	88.0	5.4	4.2

\* = dicarboxylic acid expressed in molar percent in relation to the glyoxylic acid.

### Examples 9 to 11

In the following examples, the quantity of oxalic acid used in the glyoxylic acid solution is increased.

The procedure of Example 1 is followed, and a 50% glyoxylic acid solution is used, the composition of which is given in Examples 4 to 8.

The results obtained are indicated in the following table:

Table II

Ref. ex.	Oxalic acid *	TT	RR			RT		
			para	ortho	di	para	ortho	di
9	1.00	45.2	79.5	5.1	7.6	86.7	5.6	4.1
10	1.9	47.8	80.1	4.8	8.1	83.0	5.0	4.2
11	1.78	46.1	76.5	4.8	8.0	83.0	5.2	4.3

\* = concentration of oxalic acid in % by weight in the glyoxylic acid solution.

In said table, the abbreviations, "ortho", "para" and "di" mean :

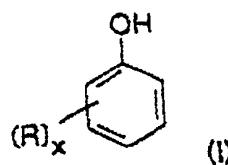
- 4-hydroxy 3-methoxy mandelic acid = para

- 2-hydroxy 3-methoxy mandelic acid = ortho
- 2-hydroxy 3-methoxy 1,5 dimandelic acid = di

CLAIMS

1 - A process for the preparation of optionally substituted p-hydroxymandelic compounds and derivatives, which consists in carrying out the condensation, in water, in the presence of an alkaline agent, of an aromatic carrier compound with at least one hydroxyl group and the para position of which is free, with glyoxylic acid, said process being characterised in that the reaction is carried out in the presence of an effective quantity of a carrier compound with at least two carboxylic functions.

2 - A process according to claim 1, characterised in that the hydroxylated compound corresponds to the following formula (I):



in which formula (I):

- the para position is free,
- x is an integer between 1 and 4,
- R represents :
  - a hydrogen atom,
  - a hydrocarbon group having from 1 to 20 carbon atoms selected from the alkyl, alkoxy, hydroxyalkyl, cycloalkyl, aryl, phenoxy, alkoxyalkyl, fluoroalkyl, hydroxyalkoxyalkylene groups,
  - a hydroxyl group,
  - a -CHO group,
  - an acyl group having from 2 to 6 carbon atoms,
  - a halogen atom, preferably a fluorine, chlorine or bromine atom,
  - two R groups placed on two vicinal carbon atoms can form together and with the carbon atoms which carry them a benzene ring.

3 - A process according to either claim 1 or claim 2, characterised in that the hydroxylated aromatic compound corresponds to formula (I), in which:

- x is equal to 0, 1, 2 or 3,

- R represents one of the following groups or functions:
  - . a hydrogen atom,
  - . a linear or branched alkyl radical having from 1 to 10 carbon atoms, and preferably from 1 to 4 carbon atoms,
  - . a linear or branched alkoxy radical having from 1 to 10 carbon atoms, preferably from 1 to 4 carbon atoms,
  - . an -OH group,
  - . a -CHO group,
  - . a halogen atom,
  - . a -CF<sub>3</sub> group.

4 - A process according to one of claims 1 to 3, characterised in that the hydroxylated aromatic compound corresponds to formula (I) in which the R radicals which are identical or different are a hydrogen atom, a linear or branched alkyl radical with 1 to 4 carbon atoms, a linear or branched alkoxy radical with 1 to 4 carbon atoms, a -CHO group, a chlorine atom, and x is preferably equal to 0 or 1.

5 - A process according to one of claims 1 to 4, characterised in that the hydroxylated aromatic compound of formula (I) is phenol, o-cresol, m-cresol, 3-ethyl phenol, 2-tert-butyl phenol, guaiacol, guetol, 2-isopropoxy phenol.

6 - A process according to one of claims 1 to 5, characterised in that the catalyst is a compound carrying at least two carboxylic functions corresponding to the following formula (II):



in which formula (II), R<sub>1</sub> represents a valency bond or an optionally substituted hydrocarbon radical containing 1 to 40 carbon atoms.

7 - A process according to claim 6, characterised in that the catalyst is a carrier compound having at least two carboxylic functions corresponding to formula (II) wherein R<sub>1</sub> symbolises a substituted or non-substituted hydrocarbon radical which can be a linear or branched, saturated or unsaturated acyclic aliphatic radical; a monocyclic or polycyclic,

saturated, unsaturated, or aromatic carbocyclic radical; a monocyclic or polycyclic, saturated, unsaturated or aromatic heterocyclic radical.

8 - A process according to claim 6, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II), in which  $R_1$  represents a linear or branched, acyclic aliphatic residue having preferably 1 to 12 carbon atoms, saturated or containing one or more unsaturations on the chain, generally 1 to 3 unsaturations which can be single or conjugated double bonds, or triple bonds; the hydrocarbon chain can optionally be:

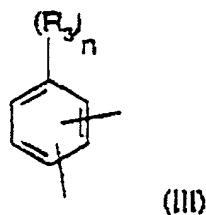
(1) - interrupted by one of the following groups called Y:  
 - O - ; - CO - ; - COO - ; - N <sub>1</sub> - ; - CO - N <sub>2</sub> - ; - S - ; - SO<sub>2</sub> -  
<sub>2</sub> <sub>2</sub>

in which formulae  $R_2$  represents hydrogen or a linear or branched alkyl radical having 1 to 4 carbon atoms, or a radical of  $-(CH_2)_p-COOH$  type in which  $p$  is a number between 1 and 5,

(2) - and/or bearing one of the following substituents:  
 - OH; - COOH ; - CHO ; - NO<sub>2</sub> ; - CN ; - NH<sub>2</sub> ; - SH ; - X ; CF<sub>3</sub>  
 - NH - [(CH<sub>2</sub>)<sub>p</sub> - COOH] or - N - [(CH<sub>2</sub>)<sub>p</sub> - COOH]<sub>2</sub>

with X representing a halogen atom, preferably a fluorine, chlorine or bromine atom, and  $p$  having the meaning given hereinabove.

9 - A process according to claim 6, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II), in which  $R_1$  represents an aromatic hydrocarbon residue, and, in particular, a benzene residue corresponding to the general formula (III):



in which formula (III):

- n is an integer from 0 to 4, preferably from 0 to 3,
- $R_3$  represents one of the following groups or functions,

- . a hydrogen atom,
- . a linear or branched alkyl radical having from 1 to 4 carbon atoms,
- . a linear or branched alkoxy radical having from 1 to 4 carbon atoms,
- . a methylene or ethylene dioxy radical,
- . a -CHO group,
- . a phenyl or benzyl radical,
- . a halogen atom.

10 - A process according to claim 6, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II) in which the R<sub>1</sub> radical represents a polycyclic aromatic hydrocarbon divalent residue; the rings can form between themselves ortho-condensed, ortho- and peri-condensed systems.

11 - A process according to claim 6, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II), in which R<sub>1</sub> represents a carbocyclic residue which is saturated or contains 1 or 2 unsaturations in the ring, generally having 3 to 7 carbon atoms, preferably 6 carbon atoms, in the ring.

12 - A process according to one of claims 6 to 11, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II), in which R<sub>1</sub> represents a divalent radical constituted by a chain formation of two to four residues as defined hereinabove, an aliphatic residue, an aromatic residue or a cycloaliphatic residue, connected together by a valency bond or by a function group.

13 - A process according to claim 6, characterised in that the catalyst is a carrier compound with at least two carboxylic functions corresponding to formula (II) selected from:

- dicarboxylic aliphatic acids, such as:

- . oxalic acid
- . malonic acid
- . succinic acid
- . glutaric acid
- . adipic acid
- . 2,4-dimethyl adipic acid
- . pimelic acid

- . suberic acid
- . azelaic acid
- . sebatic acid
- . dodecane dioic acid
- . fumaric acid
- . maleic acid
- cycloalkanedicarboxylic acids, such as cyclohexane 1,4-dicarboxylic acid,
- aromatic dicarboxylic acids, such as:
  - . phthalic acid
  - . isophthalic acid
  - . terephthalic acid
  - . phenylenediacetic acid
  - . naphthalene 1,5-dicarboxylic acid
  - . naphthalene 1,6-dicarboxylic acid
  - . 4,4'-diphenylcarboxylic acid
  - . 3,3'-diphenylcarboxylic acid
  - . bis(4-hydroxycarbonyl) phenyl oxide
  - . bis(3-hydroxycarbonyl) phenyl oxide
  - . 4,4'-dihydroxycarbonyl diphenylsulphone
  - . 3,3'-dihydroxycarbonyl diphenylsulphone
- pyrimidine or imidazole dicarboxylic acids.
- aminopolycarboxylic acids:
  - . ethylenediaminetetraacetic acid (E.D.T.A.)
  - . diethylenetriaminopentacetic acid (D.T.P.A.)
  - . nitrilotriacetic acid (N.T.A.)
  - . N-(2-hydroxyethyl)ethylene diaminotriacetic acid (H.E.D.T.A.).

14 - A process according to one of claims 1 to 13, characterised in that the aqueous solution of glyoxylic acid contains monofunctional acids, in particular from 0.1 to 3% acetic acid.

15 - A process according to one of claims 1 to 14, characterised in that the aqueous solution of glyoxylic acid has a concentration which varies from 15 to 70% by weight, preferably in the region of 50% by weight.

16 - A process according to one of claims 1 to 15, characterised in that the molar ratio between the hydroxylated aromatic compound of formula (I) and the glyoxylic acid varies between 1.5 and 4.0 and is preferably selected between 2.0 and 3.0.

17 - A process according to one of claims 1 to 16, characterised in that the quantity of alkali metal hydroxide is in the region of, or equal to, the stoichiometric quantity necessary to salfify all the salifiable groups of the hydroxylated aromatic compound of formula (I) and to salfify the carboxylic function of the glyoxylic acid.

18 - A process according to one of claims 1 to 17, characterised in that the concentration of the hydroxylated aromatic compound of formula (I) is preferably comprised between 0.5 and 1.5 moles/litre, and more particularly in the region of 1 mole/litre.

19 - A process according to one of claims 1 to 18, characterised in that the quantity of catalyst used is such that the molar ratio between the catalyst and the hydroxylated aromatic compound of formula (I) is between 0.005 and 0.025, and preferably between 0.01 and 0.02.

20 - A process according to one of claims 1 to 19, characterised in that the quantity of catalyst used, as expressed by the ratio between the number of moles of catalyst and the number of moles of glyoxylic acid, is selected between 0.5 and 2.5%, preferably between 1 and 2%.

21 - A process according to one of claims 1 to 20, characterised in that the catalyst is entirely or partly provided by the aqueous solution of glyoxylic acid.

22 - A process according to claim 21, characterised in that the solution of glyoxylic acid comprises between 0.6 and 3%, preferably between 1.2 and 2.6%, by weight, of oxalic acid, as expressed in relation to the weight of glyoxylic acid.

23 - A process according to one of claims 1 to 22, characterised in that the catalyst is introduced with the aqueous solution of glyoxylic acid or into the starting reaction medium containing the hydroxylated aromatic compound of formula (I), water and the alkali metal hydroxide.

24 - A process according to one of claims 1 to 23, characterised in that the temperature of the reaction varies between 20°C and 60°C, preferably between 30°C and 40°C.

25 - Use of the optionally substituted p-hydroxymandelic compounds obtained according to one of claims 1 to 24 as intermediates for the production of hydroxyarylacetic acids, hydroxyarylglyoxylic acids, or hydroxyaromatic aldehydes.

26 - Use of p-hydroxymandelic acid and 3-methoxy p-hydroxymandelic, 3-ethoxy p-hydroxymandelic acids or 3-isopropoxy p-hydroxymandelic acids obtained in accordance with the preparation process described in one of claims 1 to 24 for the production of 4-hydroxy benzaldehyde and vanillin and analogues by oxidation of said acids.

15 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100  
W. G. 3 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023 2024 2025 2026 2027 2028 2029 2030 2031 2032 2033 2034 2035 2036 2037 2038 2039 2040 2041 2042 2043 2044 2045 2046 2047 2048 2049 2050 2051 2052 2053 2054 2055 2056 2057 2058 2059 2060 2061 2062 2063 2064 2065 2066 2067 2068 2069 2070 2071 2072 2073 2074 2075 2076 2077 2078 2079 2080 2081 2082 2083 2084 2085 2086 2087 2088 2089 2090 2091 2092 2093 2094 2095 2096 2097 2098 2099 20100 20101 20102 20103 20104 20105 20106 20107 20108 20109 20110 20111 20112 20113 20114 20115 20116 20117 20118 20119 20120 20121 20122 20123 20124 20125 20126 20127 20128 20129 20130 20131 20132 20133 20134 20135 20136 20137 20138 20139 20140 20141 20142 20143 20144 20145 20146 20147 20148 20149 20150 20151 20152 20153 20154 20155 20156 20157 20158 20159 20160 20161 20162 20163 20164 20165 20166 20167 20168 20169 20170 20171 20172 20173 20174 20175 20176 20177 20178 20179 20180 20181 20182 20183 20184 20185 20186 20187 20188 20189 20190 20191 20192 20193 20194 20195 20196 20197 20198 20199 20200 20201 20202 20203 20204 20205 20206 20207 20208 20209 202010 202011 202012 202013 202014 202015 202016 202017 202018 202019 202020 202021 202022 202023 202024 202025 202026 202027 202028 202029 202030 202031 202032 202033 202034 202035 202036 202037 202038 202039 202040 202041 202042 202043 202044 202045 202046 202047 202048 202049 202050 202051 202052 202053 202054 202055 202056 202057 202058 202059 202060 202061 202062 202063 202064 202065 202066 202067 202068 202069 202070 202071 202072 202073 202074 202075 202076 202077 202078 202079 202080 202081 202082 202083 202084 202085 202086 202087 202088 202089 202090 202091 202092 202093 202094 202095 202096 202097 202098 202099 2020100 2020101 2020102 2020103 2020104 2020105 2020106 2020107 2020108 2020109 2020110 2020111 2020112 2020113 2020114 2020115 2020116 2020117 2020118 2020119 2020120 2020121 2020122 2020123 2020124 2020125 2020126 2020127 2020128 2020129 2020130 2020131 2020132 2020133 2020134 2020135 2020136 2020137 2020138 2020139 2020140 2020141 2020142 2020143 2020144 2020145 2020146 2020147 2020148 2020149 2020150 2020151 2020152 2020153 2020154 2020155 2020156 2020157 2020158 2020159 2020160 2020161 2020162 2020163 2020164 2020165 2020166 2020167 2020168 2020169 2020170 2020171 2020172 2020173 2020174 2020175 2020176 2020177 2020178 2020179 2020180 2020181 2020182 2020183 2020184 2020185 2020186 2020187 2020188 2020189 2020190 2020191 2020192 2020193 2020194 2020195 2020196 2020197 2020198 2020199 2020200 2020201 2020202 2020203 2020204 2020205 2020206 2020207 2020208 2020209 20202010 20202011 20202012 20202013 20202014 20202015 20202016 20202017 20202018 20202019 20202020 20202021 20202022 20202023 20202024 20202025 20202026 20202027 20202028 20202029 202020200 202020201 202020202 202020203 202020204 202020205 202020206 202020207 202020208 202020209 2020202010 2020202011 2020202012 2020202013 2020202014 2020202015 2020202016 2020202017 2020202018 2020202019 2020202020 2020202021 2020202022 2020202023 2020202024 2020202025 2020202026 2020202027 2020202028 2020202029 20202020200 20202020201 20202020202 20202020203 20202020204 20202020205 20202020206 20202020207 20202020208 20202020209 202020202010 202020202011 202020202012 202020202013 202020202014 202020202015 202020202016 202020202017 202020202018 202020202019 202020202020 202020202021 202020202022 202020202023 202020202024 202020202025 202020202026 202020202027 202020202028 202020202029 2020202020200 2020202020201 2020202020202 2020202020203 2020202020204 2020202020205 2020202020206 2020202020207 2020202020208 2020202020209 20202020202010 20202020202011 20202020202012 20202020202013 20202020202014 20202020202015 20202020202016 20202020202017 20202020202018 20202020202019 20202020202020 20202020202021 20202020202022 20202020202023 20202020202024 20202020202025 20202020202026 20202020202027 20202020202028 20202020202029 202020202020200 202020202020201 202020202020202 202020202020203 202020202020204 202020202020205 202020202020206 202020202020207 202020202020208 202020202020209 2020202020202010 2020202020202011 2020202020202012 2020202020202013 2020202020202014 2020202020202015 2020202020202016 2020202020202017 2020202020202018 2020202020202019 2020202020202020 2020202020202021 2020202020202022 2020202020202023 2020202020202024 2020202020202025 2020202020202026 2020202020202027 2020202020202028 2020202020202029 20202020202020200 20202020202020201 20202020202020202 20202020202020203 20202020202020204 20202020202020205 20202020202020206 20202020202020207 20202020202020208 20202020202020209 202020202020202010 202020202020202011 202020202020202012 202020202020202013 202020202020202014 202020202020202015 202020202020202016 202020202020202017 202020202020202018 202020202020202019 202020202020202020 202020202020202021 202020202020202022 202020202020202023 202020202020202024 202020202020202025 202020202020202026 202020202020202027 202020202020202028 202020202020202029 2020202020202020200 2020202020202020201 2020202020202020202 2020202020202020203 2020202020202020204 2020202020202020205 2020202020202020206 2020202020202020207 2020202020202020208 2020202020202020209 20202020202020202010 20202020202020202011 20202020202020202012 20202020202020202013 20202020202020202014 20202020202020202015 20202020202020202016 20202020202020202017 20202020202020202018 20202020202020202019 20202020202020202020 20202020202020202021 20202020202020202022 20202020202020202023 20202020202020202024 20202020202020202025 20202020202020202026 20202020202020202027 20202020202020202028 20202020202020202029 202020202020202020200 202020202020202020201 202020202020202020202 202020202020202020203 202020202020202020204 202020202020202020205 202020202020202020206 202020202020202020207 202020202020202020208 202020202020202020209 2020202020202020202010 2020202020202020202011 2020202020202020202012 2020202020202020202013 2020202020202020202014 2020202020202020202015 2020202020202020202016 2020202020202020202017 2020202020202020202018 2020202020202020202019 2020202020202020202020 2020202020202020202021 2020202020202020202022 2020202020202020202023 2020202020202020202024 2020202020202020202025 2020202020202020202026 2020202020202020202027 2020202020202020202028 2020202020202020202029 20202020202020202020200 20202020202020202020201 20202020202020202020202 20202020202020202020203 20202020202020202020204 20202020202020202020205 20202020202020202020206 20202020202020202020207 20202020202020202020208 20202020202020202020209 202020202020202020202010 202020202020202020202011 202020202020202020202012 202020202020202020202013 202020202020202020202014 202020202020202020202015 202020202020202020202016 202020202020202020202017 202020202020202020202018 202020202020202020202019 202020202020202020202020 202020202020202020202021 202020202020202020202022 202020202020202020202023 202020202020202020202024 202020202020202020202025 202020202020202020202026 202020202020202020202027 202020202020202020202028 202020202020202020202029 2020202020202020202020200 2020202020202020202020201 2020202020202020202020202 2020202020202020202020203 2020202020202020202020204 2020202020202020202020205 2020202020202020202020206 2020202020202020202020207 2020202020202020202020208 2020202020202020202020209 20202020202020202020202010 20202020202020202020202011 20202020202020202020202012 20202020202020202020202013 20202020202020202020202014 20202020202020202020202015 20202020202020202020202016 20202020202020202020202017 20202020202020202020202018 20202020202020202020202019 20202020202020202020202020 20202020202020202020202021 20202020202020202020202022 20202020202020202020202023 20202020202020202020202024 20202020202020202020202025 20202020202020202020202026 20202020202020202020202027 20202020202020202020202028 20202020202020202020202029 202020202020202020202020200 202020202020202020202020201 202020202020202020202020202 202020202020202020202020203 202020202020202020202020204 202020202020202020202020205 202020202020202020202020206 202020202020202020202020207 202020202020202020202020208 202020202020202020202020209 2020202020202020202020202010 2020202020202020202020202011 2020202020202020202020202012 2020202020202020202020202013 2020202020202020202020202014 2020202020202020202020202015 2020202020202020202020202016 2020202020202020202020202017 2020202020202020202020202018 2020202020202020202020202019 2020202020202020202020202020 2020202020202020202020202021 2020202020202020202020202022 2020202020202020202020202023 2020202020202020202020202024 2020202020202020202020202025 2020202020202020202020202026 2020202020202020202020202027 2020202020202020202020202028 2020202020202020202020202029 20202020202020202020202020200 20202020202020202020202020201 20202020202020202020202020202 20202020202020202020202020203 20202020202020202020202020204 20202020202020202020202020205 20202020202020202020202020206 20202020202020202020202020207 20202020202020202020202020208 20202020202020202020202020209 202020202020202020202020202010 202020202020202020202020202011 202020202020202020202020202012 202020202020202020202020202013 202020202020202020202020202014 202020202020202020202020202015 202020202020202020202020202016 202020202020202020202020202017 202020202020202020202020202018 202020202020202020202020202019 202020202020202020202020202020 202020202020202020202020202021 202020202020202020202020202022 202020202020202020202020202023 202020202020202020202020202024 202020202020202020202020202025 202020202020202020202020202026 202020202020202020202020202027 202020202020202020202020202028 202020202020202020202020202029 2020202020202020202020202020200 2020202020202020202020202020201 2020202020202020202020202020202 2020202020202020202020202020203 2020202020202020202020202020204 2020202020202020202020202020205 2020202020202020202020202020206 2020202020202020202020202020207 2020202020202020202020202020208 2020202020202020202020202020209 20202020202020202020202020202010 20202020202020202020202020202011 20202020202020202020202020202012 20202020202020202020202020202013 20202020202020202020202020202014 20202020202020202020202020202015 20202020202020202020202020202016 20202020202020202020202020202017 20202020202020202020202020202018 20202020202020202020202020202019 20202020202020202020202020202020 20202020202020202020202020202021 20202020202020202020202020202022 20202020202020202020202020202023 20202020202020202020202020202024 20202020202020202020202020202025 20202020202020202020202020202026 20202020202020202020202020202027 20202020202020202020202020202028 20202020202020202020202020202029 202020202020202020202020202020200 202020202020202020202020202020201 202020202020202020202020202020202 202020202020202020202020202020203 202020202020202020202020202020204 202020202020202020202020202020205 202020202020202020202020202020206 202020202020202020202020202020207 202020202020202

## DEMANDE INTERNATIONALE PUBLIEE EN VERTU DU TRAITE DE COOPERATION EN MATIERE DE BREVETS (PCT)

(51) Classification internationale des brevets <sup>6</sup> : <b>C07C 51/367, 59/64, 59/52, 51/377, 45/67</b>		A1	(11) Numéro de publication internationale: <b>WO 99/65853</b> (43) Date de publication internationale: 23 décembre 1999 (23.12.99)
(21) Numéro de la demande internationale: PCT/FR99/01442			(81) Etats désignés: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, brevet ARIPO (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), brevet eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), brevet européen (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), brevet OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(22) Date de dépôt international: 16 juin 1999 (16.06.99)			
(30) Données relatives à la priorité: 98/07586 16 juin 1998 (16.06.98) FR			
(71) Déposant ( <i>pour tous les Etats désignés sauf US</i> ): RHO-DIA CHIMIE [FR/FR]; 25, quai Paul Doumer, F-92408 Courbevoie Cedex (FR).			
(72) Inventeurs; et			
(75) Inventeurs/Déposants ( <i>US seulement</i> ): JOUVE, Isabelle [FR/FR]; 4, rue Bossuet, F-69740 Genas (FR). FOURNET, Frédéric [FR/FR]; 18, montée Lyvet, F-69270 Couzon au Mont d'Or (FR). FRAGNON, Jean [FR/FR]; 6, rue Théophile Gautier, F-69330 Meyzieu (FR).			Publiée <i>Avec rapport de recherche internationale.</i>
(74) Mandataire: DUTRUC-ROSSET, Marie-Claude; Rhodia Services, Direction de la Propriété Industrielle, 25, quai Paul Doumer, F-92408 Courbevoie Cedex (FR).			

(54) **Title: METHOD FOR PREPARING P-HYDROXYMANDELIC COMPOUNDS OPTIONALLY SUBSTITUTED**

(54) **Titre: PROCEDE DE PREPARATION DE COMPOSES P-HYDROXYMANDELIQUES EVENTUELLEMENT SUBSTITUES**

(57) **Abstract**

The invention concerns a method for preparing p-hydroxymandelic compounds optionally substituted and their derivatives. More particularly, it concerns a method for preparing p-hydroxymandelic acid and methoxy-3 p-hydroxymandelic acid and their derivatives. The invention concerns a method for preparing p-hydroxymandelic compounds optionally substituted and their derivatives, which consists in condensing in water, in the presence of an alkaline agent, an aromatic compound bearing at least a hydroxyl group and whereof the position in para is free, with glyoxylic acid, said method being characterised in that the reaction is carried out in the presence of an efficient amount of a compound bearing at least two carboxylic functions.

(57) **Abrégé**

La présente invention a pour objet un procédé de préparation de composés p-hydroxymandéliques éventuellement substitués et dérivés. Elle vise plus particulièrement la préparation de l'acide p-hydroxymandélique et de l'acide méthoxy-3 p-hydroxymandélique et dérivés. L'invention a pour objet un procédé de préparation de composés p-hydroxymandéliques éventuellement substitués et dérivés qui consiste à effectuer la condensation dans l'eau, en présence d'un agent alcalin, d'un composé aromatique porteur d'au moins un groupe hydroxyle et dont la position en para est libre, avec l'acide glyoxylique, ledit procédé étant caractérisé par le fait que la réaction est conduite en présence d'une quantité efficace d'un composé porteur d'au moins deux fonctions carboxyliques.

**COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY  
(Includes Reference to Provisional and PCT International Applications)**

Attorney's Docket No.  
022701-907

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;  
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**METHOD FOR PREPARING P-HYDROXYMANDELIC COMPOUNDS OPTIONALLY SUBSTITUTED**

the specification of which (check only one item below):

is attached hereto.  
 was filed as United States application

Number \_\_\_\_\_  
on \_\_\_\_\_  
and was amended  
on \_\_\_\_\_ (if applicable).

was filed as PCT international application

Number PCT/FR99/01442  
on 16 June 1999  
and was amended  
on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(e) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

**PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. §119:**

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 U.S.C. §119
FR	98/07586	16 June 1998	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

\_\_\_\_\_ (Application Number)

\_\_\_\_\_ (Filing Date)

\_\_\_\_\_ (Application Number)

\_\_\_\_\_ (Filing Date)

**COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONT'D)**  
 (Includes Reference to Provisional and PCT International Applications)

Attorney's Docket No.  
 022701-907

I hereby claim the benefit under Title 35, United States Code, §120 of any United States applications(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the Office all information known to me to be material to the patentability as defined in Title 37, Code of Federal Regulations §1.56, which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. §120:

U.S. APPLICATIONS		STATUS (check one)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED
<b>PCT APPLICATIONS DESIGNATING THE U.S.</b>				
PCT APPLICATION NO.	PCT FILING DATE	U.S. APPLICATION NUMBERS ASSIGNED (if any)		

I hereby appoint the following attorneys and agent(s) to prosecute said application and to transact all business in the Patent and Trademark Office connected therewith and to file, prosecute and to transact all business in connection with international applications directed to said invention:

William L. Mathis	17,337	Eric H. Weisblatt	30,505	Bruce T. Wieder	33,815
Robert S. Swecker	19,885	James W. Peterson	26,057	Todd R. Walters	34,040
Platon N. Mandros	22,124	Teresa Stanek Rea	30,427	Ronni S. Jillions	31,979
Benton S. Duffett, Jr.	22,030	Robert E. Krebs	25,885	Harold R. Brown III	36,341
Norman H. Stepno	22,716	William C. Rowland	30,888	Allen R. Baum	36,086
Ronald L. Grudziecki	24,970	T. Gene Dillahunt	25,423	Steven M. duBois	35,023
Frederick G. Michaud, Jr.	26,003	Patrick C. Keane	32,858	Brian P. O'Shaughnessy	32,747
Alan E. Kopecki	25,813	B. Jefferson Boggs, Jr.	32,344	Kenneth B. Leffler	36,075
Regis E. Slutter	26,999	William H. Benz	25,952	Fred W. Hathaway	32,236
Samuel C. Miller, III	27,360	Peter K. Skiff	31,917	Wendi L. Weinstein	34,456
Robert G. Mukai	28,531	Richard J. McGrath	29,195	Mary Ann Dillahunt	34,576
George A. Hovanec, Jr.	28,223	Matthew L. Schneider	32,814		
James A. LaBarre	28,632	Michael G. Savage	32,596		
E. Joseph Gess	28,510	Gerald F. Swiss	30,113		
R. Danny Huntington	27,903	Charles F. Wieland III	33,096		



**21839**

and:

Address all correspondence to:



**21839**

Norman H. Stepno  
 BURNS, DOANE, SWECKER & MATHIS, L.L.P.  
 P.O. Box 1404  
 Alexandria, Virginia 22313-1404

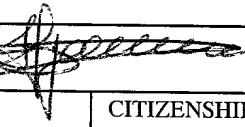
Address all telephone calls to: Norman H. Stepno at (703) 836-6620.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONT'D)  
(Includes Reference to Provisional and PCT International Applications)

Attorney's Docket No.

022701-907

FULL NAME OF SOLE OR FIRST INVENTOR Isabelle JOUVE		SIGNATURE 	DATE 02/01/01
RESIDENCE 4, rue Bossuet, F-69740 Genas, FR		CITIZENSHIP FR	
POST OFFICE ADDRESS 4, rue Bossuet, F-69740 Genas, FR			
FULL NAME OF SECOND JOINT INVENTOR, IF ANY Frederic FOURNET		SIGNATURE 	DATE 02/14/01
RESIDENCE 18, montee Lyvet, F-69270 Couzon au Mont d'Or, FR		CITIZENSHIP FR	
POST OFFICE ADDRESS 18, montee Lyvet, F-69270 Couzon au Mont d'Or, FR			
FULL NAME OF THIRD JOINT INVENTOR, IF ANY Jean FRAGNON		SIGNATURE 	DATE 6/02/01
RESIDENCE 6, rue Theophile Gautier, F-69330 Meyzieu, FR		CITIZENSHIP FR	
POST OFFICE ADDRESS 6, rue Theophile Gautier, F-69330 Meyzieu, FR			
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY		SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY		SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF SIXTH JOINT INVENTOR, IF ANY		SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF SEVENTH JOINT INVENTOR, IF ANY		SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
FULL NAME OF EIGHTH JOINT INVENTOR, IF ANY		SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			